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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,447	07/24/2003	Yadong Huang	GLAD-281	3423

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
01/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/627,447	HUANG, YADONG	
	Examiner	Art Unit	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 November 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-8,10-14,19 and 20*.
   Claim(s) withdrawn from consideration: *15-18,21 and 22*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). ____

13. ☐ Other: _____.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments are not persuasive. Applicant argues that studies have shown that apoE synthesized by the liver does not enter the brain from the plasma; and that apoE synthesized in the brain does not enter the plasma, and Applicant cites Linton et al. in support of this. Applicant also states that Huan indicates that carboxyl terminal-truncated apoE is insoluble and was found intracellularly, and furthermore that production of carboxyl terminal-truncated apoE in the body has been shown to be nuron specific, and cites Brecht et al. in support of this. Applicant argues that it thus cannot be reasoanbly concluded, from a disclosure that apoE4 can be detected in bodily fluids such as blood, that carboxyl-terminal truncated apoE produced by the brain would also be present in an aqueous biological sample such as blood or serum. Examiner notes however that nothing in the literature, including Applicant's cited prior art disclose or suggest that no apoE produced by the brain would also be present in blood or serum. To the contrary, Linton states in the abstract that the data evidenced that greater than 90% of the apoE in the plasma is synthesized by the liver, and the data also indicates that most of the apoE in CSF canno be derived from the plasma pool and therefore must be synthesized locally. Thus, there is no indication that apoE synthesized in the brain cannot be in plasma, but rather appears to suggest that apoE in plasma (10%) may be synthesized elsewhere other than the liver. Furthermore, it is emphasized that the motivation for the skilled artisan to modify a known invention need not be explicitly stated in a reference, but rather the reasons for a modification can be based on what the skilled artisan would reasonably understand or be ordinarily motivated to do. As stated in the last Office action, Roses et al. disclose that apoE are found also in blood, blood serum, blood plasma, cerebrospinal fluid, or other tissues (col. 9, line 66 - col. 10, line 2), and that apoE found in these samples can be used to as markers for the diagnosis of Alzheimer's disease (col. 3, lines 55-59.) Thus, Roses et al. suggest that regardless of where the apoE is synthesized, it can be used to diagnose Alzheimer's disease in the various biological fluids and tissues where it can be found. Because Roses et al. disclose that bodily fluids such as blood and cerebrospinal fluid as well as tissues contain apoE and can be used in diagnosing Alzheimer's disease, the skilled artisan would be suggested to detect in non-tissue samples also the carboxyl-terminated apoE as disclosed by Huang et al. as a marker for Alzheimer's disease. Moreover, it is understood in the art that such bodily samples can be obtained from living patients and are more readily obtainable than tissue samples or cell lysates, which provides a motivation for the skilled artisan to detect the carboxyl-terminated apoE in such fluid samples as a marker for Alzheimer's disease.